



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,136	10/12/2000	John F. Engelhardt	875.032US1	7933

21186 7590 02/24/2003

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.  
P.O. BOX 2938  
MINNEAPOLIS, MN 55402

EXAMINER

SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
----------	--------------

1636

DATE MAILED: 02/24/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/689,136

Applicant(s)

ENGELHARDT ET AL.

Examiner

Daniel M Sullivan

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-86 is/are pending in the application.
- 4a) Of the above claim(s) 13-28 and 37-82 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12, 29-36 and 83-86 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 December 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This Office Action is a response to the "Amendment and Response" filed 2 December 2002 (Paper No. 13) in reply to the Non-Final Office Action mailed 26 June 2002 (Paper No. 10). Claims 13-28 and 37-82 were withdrawn and claims 1-12, 29-36, 83 and 84 were considered in Paper No. 10. Claims 1, 6 and 12 were amended and claims 85 and 86 were added in paper No. 13. Claims 1-86 are pending and claims 1-12, 29-36 and 83-86 are considered herein.

#### ***Election/Restrictions***

This application contains claims drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Please note that the response must also include amendments to claims 29 and 83 such that they no longer depend from non-elected claims 13-17.

#### ***Response to Amendment***

##### **Drawings**

Objection to the drawings is withdrawn in view of the filing of formal drawings (Paper No. 11).

##### **Specification**

Objection to the specification is withdrawn in view of the amendments thereto in Paper No. 13.

Claim Rejections - 35 USC § 112

Rejection of claims 7, 8 and 12 under 35 U.S.C. § 112, second paragraph, is withdrawn in view of the arguments of record in Paper No. 13 regarding claims 7 and 8, and in view of the amendment of claim 12.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 4, 5 and 10-12 under 35 U.S.C. § 102(b) as anticipated by any one of Alexander *et al.*, Russell *et al.*, Halbert *et al.* or Kessler *et al.* is withdrawn in view of the amendment to claim 1 such that the claims are now limited to agents that alter transduction after viral binding to receptors and before synthesis to an expressible form of the viral genome.

Claims 1, 4, 5 and 10-12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Qing *et al.* for reasons of record in Paper No. 10. The agent of Qing *et al.* acts to relieve inhibition of viral single-strand DNA synthesis by ssD-BP, which occurs after viral binding to receptors and before synthesis of an expressible form of the viral genome (see especially Figure 7 and the caption thereto). The agent taught by Qing *et al.* is encompassed by the agent of the claims; therefore, the method of Qing *et al.* still anticipates the amended claims for the reasons of record.

Claim Rejections - 35 USC § 103

Rejection of claims 1, 3-5, 10 and 11 under 35 U.S.C. § 103(a) as unpatentable over Alexander *et al.* in view of Snyder *et al.* is withdrawn in view of the amendment to claim 1 such

Art Unit: 1636

that the claims are now limited to agents that alter transduction after viral binding to receptors and before synthesis to an expressible form of the viral genome.

***New Grounds for Rejection Necessitated by Amendment***

Claim Rejections - 35 USC § 112

Claims 1-12, 29-36 and 83-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1, as amended in Paper No. 13, is directed to a method comprising contacting a mammalian cell with an agent that alters transduction of a mammalian cell after viral binding to receptors. There is no support for this limitation in the disclosure as filed. The passage cited by Applicant for support (i.e. page 20, lines 23-33) teaches binding of the virus to the cell membrane. Amending the claim to substitute “the cell membrane” for “receptors” would be remedial.

Claims 1-6, 9-12, 83, 84 and 86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

Art Unit: 1636

in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

The claims, as amended in Paper No. 13, are directed to a method to identify an agent that alters adeno-associated virus (AAV) transduction of a mammalian cell, wherein said agent is limited to an agent that alters transduction after viral binding to receptors and before synthesis to an expressible form of the viral genome or, in more limited embodiments, to an agent that enhances endosomal processing. The Guidelines for Written Description state “The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art” (Federal Register, Vol. 66, No. 4, Column 3, page 71434). In the instant case, the agent that alters transduction after viral binding to receptors and before synthesis to an expressible form of the viral genome or enhances endosomal processing is a critical element of the method, as the method is limited to agents having only those properties. Therefore, adequate description of the claimed method requires adequate written description of the agent.

In the third full paragraph on page 20, the specification teaches that the process of transduction comprises 1) binding of the virus to the cell membrane, 2) endocytosis, 3) escape from endosomes and trafficking to the nucleus, 4) uncoating of the virus particles and synthesis of the second DNA strand to form expressible double-strand forms, including circular intermediates, and 5) integration into the host genome. The agent of the claims can alter transduction at any of steps 2, 3 or 4. Thus, the agent encompasses a genus of compounds

Art Unit: 1636

capable of altering endocytosis, escape from endosomes, trafficking to the nucleus, uncoating of virus particles and synthesis of the second DNA strand. Given that each of these processes is distinct and involves unique cellular components, the genus of compounds encompassed by the agent must be highly divergent.

The Guidelines for Written Description state “when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus”, “In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus” (Federal Register, Vol. 66, No. 4, Column 2, page 71436). The disclosure does not provide a single example of agents capable of altering virus trafficking to the nucleus, uncoating of virus particles or synthesis of the second viral DNA strand. Therefore, the skilled artisan could not possibly envision agents capable of altering trafficking, uncoating or second strand synthesis based on the teachings of the instant disclosure.

With regard to endocytosis and endosomal processing, the instant disclosure provides only a single example of an agent that alters endocytosis (i.e. brefeldin A; page 45) and examples of compounds capable of altering, or enhancing, endosomal processing that fall into two classes (i.e. endosomal protease inhibitors and ubiquitin ligase inhibitors). However, given the complexity of endocytosis and endosomal processing (evidenced by Alberts *et al.* (1994) Molecular Biology of the Cell, third edition, Garland Publishing, Inc. New York, pages 618-626), the skilled artisan would expect that genus of compounds capable of altering endocytosis or endosomal processing is highly divergent and would encompass many compounds outside of

Art Unit: 1636

those that are represented by brefeldin A, endosomal protease inhibitors, or ubiquitin ligase inhibitors.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of compounds capable of altering transduction after viral binding to receptors and before synthesis to an expressible form of the viral genome. Therefore, only the described brefeldin A, endosomal protease inhibitors and ubiquitin ligase inhibitors meet the written description provision of 35 U.S.C. §112, first paragraph.

Further, as claim 83 is directed to administering an agent that enhances the activity of the agent of claim 1, and claim 1 is now directed to agents having defined activity, adequate written description for claim 83 requires description of the genus of compounds that are capable of enhancing each of the activities encompassed by the agent of claim 1. The instant disclosure provides a single example of an agent that is capable of enhancing the activity of endosomal protease inhibitors (i.e. EGTA). Clearly this example is not representative of all compounds capable of enhancing the wide range of compounds encompassed by the agent of claim 1. Therefore only EGTA meets the written description requirement for a second agent that enhances the activity of the agent of claim 1.



***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Application/Control Number: 09/689,136  
Art Unit: 1636

Page 9

dms  
February 18, 2003



**JAMES KETTER**  
**PRIMARY EXAMINER**